

The present independent claims (claims 25-27) are drawn to methods of processing blood where blood is removed from the subject at a selected removal flow rate and returned to the subject at a selected return flow rate, wherein the blood removal flow rate and/or the blood return flow rate are adjusted during operation of the blood processing procedure based on the subject's total blood volume. Specifically, claim 25 states, "removing blood from said subject at a selected removal flow rate thereby generating removed blood, wherein said selected removal flow rate is adjusted during operation of the blood processing procedure based on said total blood volume." and claim 26 reads "returning at least a portion of said return component to said subject at a selected return flow rate, wherein said selected return flow rate is adjusted during operation of the blood processing procedure based on said total blood volume of said subject." Claim 27 contains both limitations and requires that both the blood removal flow rate and return flow rate are adjusted during operation of the blood processing procedure.

To establish a prima facie case of obviousness, there must be some suggestion or motivation to combine or adapt the references; a reasonable expectation of success; and the final combination must teach or suggest all of the claim limitations. See MPEP 2142. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Applicant submits that this obviousness rejection should be withdrawn because the references cited by the Examiner do not teach or suggest either adjusting the blood removal flow rate or adjusting the blood return flow rate during operation of the blood processing procedure, and therefore do not teach or suggest all of the claim limitations.

Applicant has previously presented arguments that Holmes et al. does not disclose adjusting the blood removal rate or return rate based on the patient's total blood volume. The Examiner apparently has agreed with Applicant's arguments and states on page 3 of the Office Action that "Holmes fails to disclose the step of adjusting a removal and/or return flow rate during the blood processing procedure based on the total blood volume."

However, the Examiner asserts that the present claims are obvious over Holmes et al. in combination with Elgas.

Elgas discloses a method of tracking a patient's blood volume during cardiac surgery where a heart-lung machine drains blood from the patient, oxygenates the blood, and pumps the blood back to the patient. The patient's blood volume is monitored through the use of a marker substance injected into the patient's bloodstream. If the total blood volume in the patient's circulatory system is too low, corrective steps, such as the administration of intravenous fluids, blood transfusions or blood vessel constricting medication, can be taken to stabilize the blood volume (column 1, lines 43-47).

However, it should be noted that the patient's blood volume is not adjusted by increasing the blood return flow rate or decreasing the blood removal flow rate of the heart-lung machine in Elgas. Nowhere does Elgas disclose adjusting the blood return flow rate or removal flow rate of the device. Thus, even if one skilled in the art were to combine Holmes et al. and Elgas, the resulting method would not produce all of the claim limitations. Specifically, the combination of Elgas and Holmes et al. does not result in adjusting the blood removal flow rate or return flow rate during operation of the blood processing procedure as required by the present claims.

While Elgas teaches that the patient's blood volume should be monitored and corrective steps taken if the blood volume becomes too low, there is no teaching or suggestion that this should be accomplished by adjusting the blood removal rate and/or return rate. In fact, Elgas teaches away from the present invention by teaching that low circulation volume is corrected through the separate administration of another fluid or through medication as opposed to reducing the blood removal flow rate or increasing the blood flow return rate. One method of maintaining the correct circulatory system volume in the patient as taught by Elgas is through the administration of intravenous fluids. However, as shown in Figure 1 of Elgas, the IV bag (item 14) and the IV pump (item 16) are physically separate from the device removing and returning the patient's blood. The infusion of intravenous fluids in Elgas is a separate process and does not involve adjusting the blood

removal rate or return rate. Another alternative taught by Elgas is to provide the patient with a blood transfusion, particularly if the drop in volume is caused by blood loss during surgery (column 1, lines 43-47). The other alternative taught by Elgas is to administer medication to the patient where the loss in circulatory system volume is caused by kidney activity or expansion of blood vessels (column 1, lines 42-47). Again, these methods do not involve adjusting the blood removal flow rate or return flow rate of the device performing the blood processing operation.

Additionally, Applicant notes that the device in Elgas is heart-lung machine which is used to oxygenate and circulate blood through the body during heart surgery. The patient's requirement for proper blood circulation through the body will remain fairly constant. Thus, disruptions or changes to the blood flow to and from the heart-lung machine could lead to disastrous and life threatening results. Accordingly, one skilled in the art would not consider adjusting the blood removal flow rate or return flow rate as a means of correcting low total blood volume in Elgas. Instead one skilled in the art would utilize one of the methods taught by Elgas.

Because Elgas does not disclose adjusting the blood removal rate and/or return rate as a means for correcting blood volume; and provides alternative methods for correcting blood volume; and because adjusting the blood removal rate and return rate would be inoperative with the procedure in Elgas, one skilled in the art would not find a teaching or suggestion from Elgas to add the adjustment of the blood removal flow rate or return flow rate to the device and method taught in Holmes et al. to reach the limitations required by independent claims 25-27. Accordingly, this rejection should be withdrawn. Since independent claims 25-27 are not obvious over Holmes et al. and Elgas, the remaining claims which depend from these claims also are not obvious and should be allowed.

The Examiner makes additional rejections to the dependent claims as being obvious over Holmes et al. and Elgas. Applicant submits that the present independent claims are not obvious over Holmes et al. and Elgas for the reasons stated above which obviates the

Examiner's further rejections, however additional rejections by the Examiner are addressed below.

With regard to claims 3-10, and 28-39, these claims recite methods where the return flow rate and removal flow rate are adjusted according to specific characteristics (i.e., in a substantially linear or exponential manner) or specific equations. The Examiner rejects these claims as a result-effective variable, the mere optimization of which involves only routine skill in the art (MPEP 2144.05). As presented above, Holmes et al. and Elgas does not disclose using total blood volume to adjust the blood return rate or removal rate during operation of the blood processing procedure. MPEP 2144.05, relied upon by the Examiner, requires that:

"A particular parameter must first be recognized as a result effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of such variable might be characterized as routine experimentation. In re Antoine, 559 F.2d 618, 195 USPQ 6 (CCPA 1977) (The claimed wastewater treatment device had a tank volume to contractor area of 0.12 gal./sq.ft. The prior art did not recognize that treatment capacity is a function of the tank volume to contractor ratio, and therefore the parameter optimized was not recognized in the art to be a result-effective variable.)"

The prior art, particularly Holmes et al. and Elgas, has not recognized that blood return flow rate and removal flow rate can be beneficially varied according to total blood volume of the donor. Thus, total blood volume has not been recognized as a result effective variable which achieves a recognized result, in this case the adjusted blood removal flow rate and blood return flow rate, and so the requirements of MPEP2144.05 have not been met. Furthermore, the specification provides results which are not taught or suggested in Holmes et al. or Elgas, namely that the claimed methods demonstrate improvement in performance over the prior art (see the specification on page 31, line 16, through page 32, line 4). Accordingly, these obviousness rejections of claims 3-10, and 28-39 over Holmes et al. and Elgas should also be withdrawn.

Claims 13, 16, 41, 46 and 51-53 and 56-68 are rejected under 35 U.S.C. §103 as being obvious over Holmes et al., in view of Elgas and U.S. 6,730,054 (Pierce et al.). Applicants believe these dependent claims are allowable over Holmes et al. and Elgas with their parent claims (claims 25-27) for the reasons stated above. Pierce et al. does not overcome the deficiencies of Holmes et al. and Elgas, namely that none of these cited references teach or suggest adjusting the blood removal flow rate or return flow rate of the device during the blood processing procedure. Therefore it is believed all of the claims should be allowable. In addition, it is believed that claims 57-62 and 68 have further grounds for patentability.

Claims 57 and 58 recite specific hematocrit values for the recirculated blood component. The Examiner rejected claims 57 and 58 as being mere optimization of a result-effective variable, stating that Pierce et al. discloses that the amount of fluid supplied to the recirculation loop is sufficient to establish desired conditions in the blood separation system. However, Pierce et al. does not provide any direction or teaching how hematocrit ratios could be used to produced desirable results or even what these desirable results would be. As previously discussed, under MPEP 2144.05 a particular parameter must first be recognized as a result effective variable, i.e., a variable which achieves a recognized result, before the determination of mere optimization can be made. Pierce et al. makes no teaching that hematocrit ratios are a variable which can be used to control the efficacy of a blood separation device. Accordingly, this rejection does not comply with MPEP 2144.05 and should be withdrawn.

Similarly, the Examiner rejects claims 59-62 and 68 because the selection of variable parameters such as duration of the draw and return cycles are also allegedly mere optimization of a result-effective variable. Again, Pierce et al. makes no showing that draw and return time ratios or draw and return flow ratios are variables that are recognized to achieve a particular result. Therefore, it is improper under MPEP 2144.05 to treat the claim limitations as mere optimization of result-effective variables. Accordingly, this rejection should be withdrawn.

Applicant believes the above arguments show that each and every claim limitation of the present claims is not taught or suggested by Holmes et al. in combination with Elgas or Pierce et al. Namely, none of the cited references actually teach or suggest adjusting the blood removal flow rate and/or return flow rate during the operation of the blood processing procedure based on the subject's total blood volume. Accordingly, Applicant requests the obvious rejections under 35 U.S.C. 103 be withdrawn.

#### Conclusion

In view of the foregoing, it is submitted that this case is in condition for allowance, and passage to issuance is respectfully requested. If there are further issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

It is believed that this submission does not require the payment of fees. However, if this is incorrect, please charge any fees necessary to make this Response timely to Deposit Account No. 07-1969.

Respectfully submitted,

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